Network Systems
Science & Advanced
Computing

Biocomplexity Institute & Initiative

University of Virginia

Estimation of COVID-19 Impact in Virginia

November 16th, 2022

(data current to November 12th – November 15th)
Biocomplexity Institute Technical report: TR BI-2022-1780







About Us

- Biocomplexity Institute at the University of Virginia
 - Using big data and simulations to understand massively interactive systems and solve societal problems
- Over 20 years of crafting and analyzing infectious disease models
 - Pandemic response for Influenza, Ebola, Zika, and others



Points of Contact

Bryan Lewis brylew@virginia.edu

Srini Venkatramanan srini@virginia.edu

Madhav Marathe marathe@virginia.edu

Chris Barrett@virginia.edu

Model Development, Outbreak Analytics, and Delivery Team

Przemyslaw Porebski, Joseph Outten, Brian Klahn, Alex Telionis, Srinivasan Venkatramanan, Bryan Lewis, Aniruddha Adiga, Hannah Baek, Chris Barrett, Jiangzhuo Chen, Patrick Corbett, Stephen Eubank, Galen Harrison, Ben Hurt, Dustin Machi, Achla Marathe,

Madhav Marathe, Mark Orr, Akhil Peddireddy, Erin Raymond, James Schlitt, Anil Vullikanti,

Lijing Wang, James Walke, Andrew Warren, Amanda Wilson, Dawen Xie



Overview

• Goal: Understand impact of COVID-19 mitigations in Virginia

Approach:

- Calibrate explanatory mechanistic model to observed cases
- Project based on scenarios for next 4 months
- Consider a range of possible mitigation effects in "what-if" scenarios

Outcomes:

- Ill, Confirmed, Hospitalized, ICU, Ventilated, Death
- Geographic spread over time, case counts, healthcare burdens

Key Takeaways

Projecting future cases precisely is impossible and unnecessary. Even without perfect projections, we can confidently draw conclusions:

- Case rates and hospitalizations remain relatively flat
- VA weekly case rate is down to 72/100K from 81/100K (potential surveillance artifacts)
 - US weekly case rate is flat remaining at 73 per 100K from 74 per 100K
- VA hospital occupancy is slightly down (rolling 7 day mean of 478 from 482 a week ago) though admissions are up
 - Influenza hospitalization shows an increase in admissions though growth has stalled, however, with over 300 hospitalizations in the last week
- Projections anticipate increases in cases and hospitalizations in coming weeks
 - Combined Hospitalizations due to Influenza and COVID-19 expected to increase in short-term
- Model updates:
 - Variant X candidates have now reached 50% (BQ.1.1, BN.1, BF.7 and others and XBB among others), 50% remains at Nov 12th
 - Modified Booster Scenarios: Current pace (included in all scenarios) with comparisons between Optimistic rollout and a more Pessimistic scenario where vaccination halts at current levels

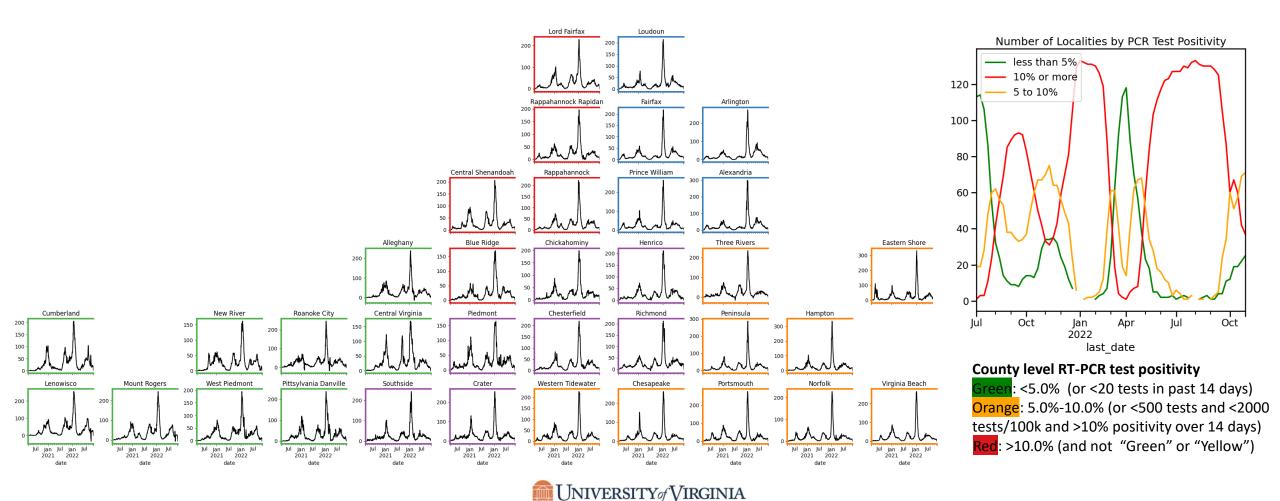
The situation continues to change. Models continue to be updated regularly.

18-Nov-22

Situation Assessment



Case Rates (per 100k) and Test Positivity

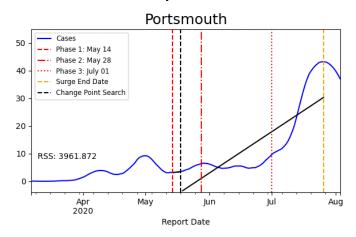


District Trajectories

Goal: Define epochs of a Health District's COVID-19 incidence to characterize the current trajectory

Method: Find recent peak and use hockey stick fit to find inflection point afterwards, then use this period's slope to define the trajectory

Hockey stick fit



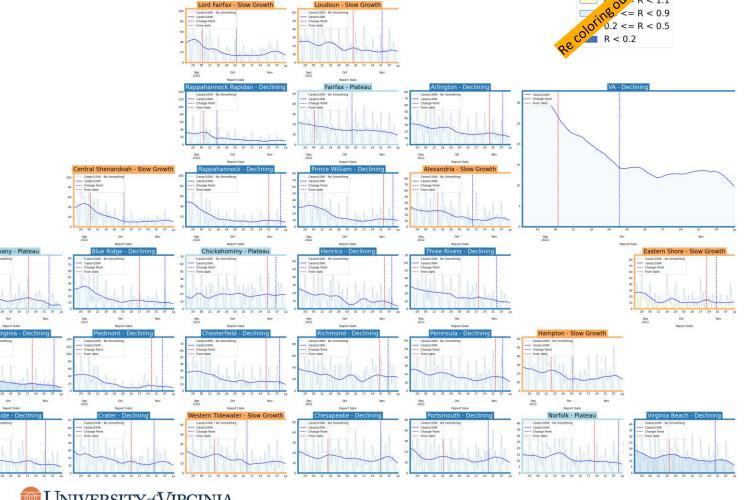
Trajectory	Description	Weekly Case Rate Slope (per 100k)	Weekly Hosp Rate Slope (per 100k)
Declining	Sustained decreases following a recent peak	slope < -0.88/day	slope < -0.07/day
Plateau	Steady level with minimal trend up or down	-0.88/day < slope < 0.42/day	-0.07/day < slope < 0.07/day
Slow Growth	Sustained growth not rapid enough to be considered a Surge	0.42/day < slope < 2.45/day	0.07/day < slope < 0.21/day
In Surge	Currently experiencing sustained rapid and significant growth	2.45/day < slope	0.21/day < slope



District Case Trajectories – last 10 weeks

Status	Number of Districts		
Status	Current Week	Last Week	
Declining	22	(11)	
Plateau	4	(7)	
Slow Growth	9	(15)	
In Surge	0	(2)	

Curve shows smoothed case rate (per 100K) Trajectories of states in label & chart box Case Rate curve colored by Reproductive number



District Hospital Trajectories – last 10 weeks

Hospitalization by county is

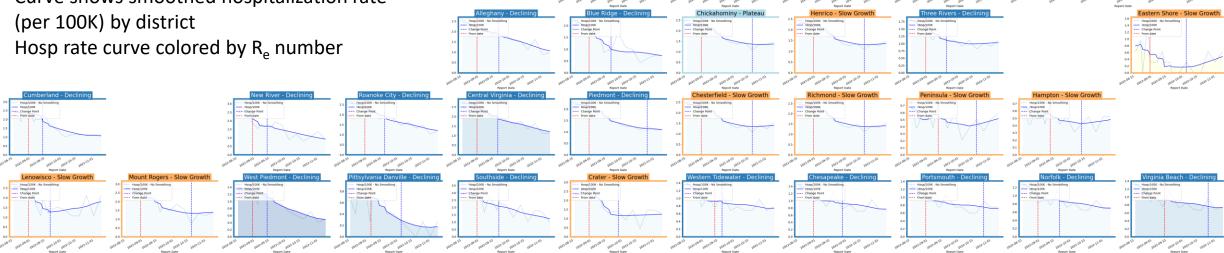
delayed, these data are

November 1st

current as of

Status	Number of Districts		
Status	Current Week	Last Week	
Declining	23	(29)	
Plateau	2	(2)	
Slow Growth	10	(4)	
In Surge	0	(0)	

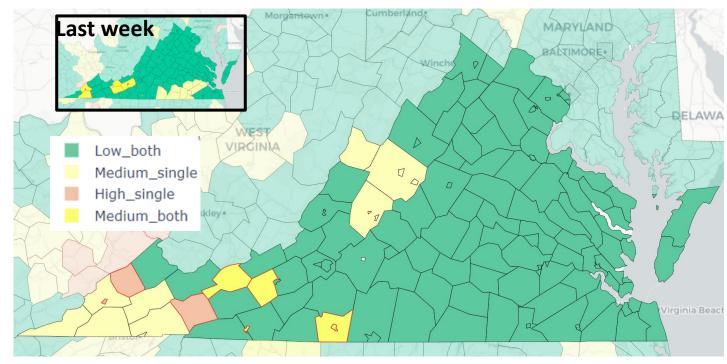
Curve shows smoothed hospitalization rate

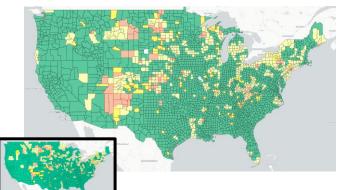


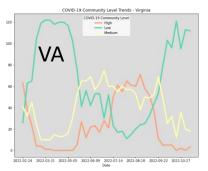
1617-08-15 1617-08-01 1617-08-15 1617-16-15 1617-16-15 1617-15-15 1617-15-15

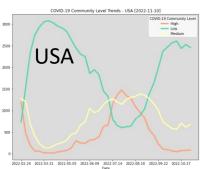
2022-11-08

CDC's COVID-19 Community Levels









MIVERSITY VIRGINIA

Red outline indicates county had 200 or more cases per 100k in last week

Pale color indicates either beds or occupancy set the level for this county

Dark color indicates both beds and occupancy set the level for this county

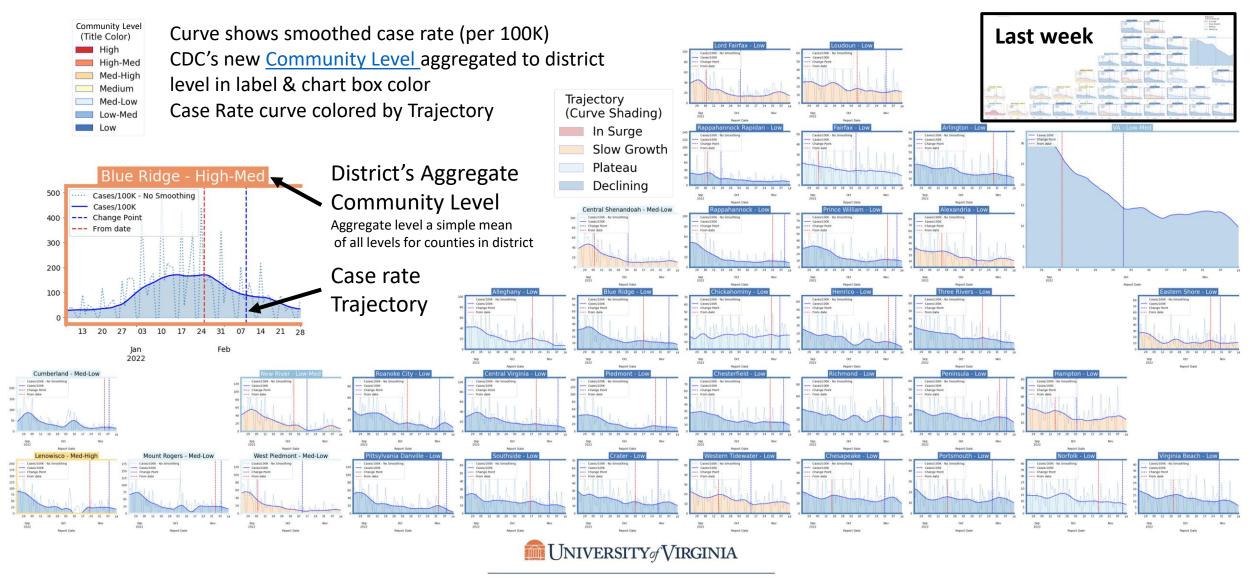
COVID-1	9 Community Levels – Use the Highest L	evel that Applies	to Your Commun	iity
New COVID-19 Cases Per 100,000 people in the past 7 days	Indicators	Low	Medium	High
	New COVID-19 admissions per 100,000 population (7-day total)	<10.0	10.0-19.9	≥20.0
Fewer than 200	Percent of staffed inpatient beds occupied by COVID-19 patients (7-day average)	<10.0%	10.0-14.9%	≥15.0%
	New COVID-19 admissions per 100,000 population (7-day total)	NA	<10.0	≥10.0
200 or more	Percent of staffed inpatient beds occupied by COVID-19 patients (7-day average)	NA	<10.0%	≥10.0%

The COVID-19 community level is determined by the higher of the new admissions and inpatient beds metrics, based on the current level of new cases per 100,000 population in the past 7 days

Data from: CDC Data Tracker Portal

Last week

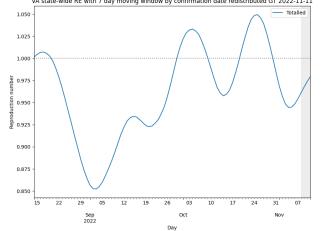
District Trajectories with Community Levels

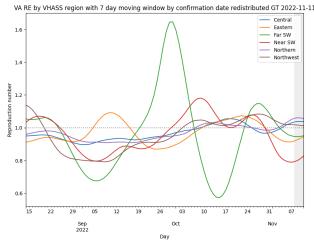


Estimating Daily Reproductive Number – Redistributed gap

Nov 11th Estimates (shifted to avoid Veterans day effect)

Region	Date Confirmed R _e	Date Confirmed Diff Last Week
State-wide	0.979	0.073
Central	1.037	0.153
Eastern	0.945	-0.001
Far SW	0.951	-0.015
Near SW	0.828	0.034
Northern	1.056	0.108
Northwest	1.012	0.015

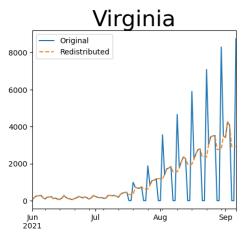




Skipping Weekend Reports & holidays biases estimates
Redistributed "big" report day to fill in gaps, and then estimate R from
"smoothed" time series

Methodology

- Wallinga-Teunis method (EpiEstim¹) for cases by confirmation date
- Serial interval: updated to discrete distribution from observations (mean=4.3, Flaxman et al, Nature 2020)
- Using Confirmation date since due to increasingly unstable estimates from onset date due to backfill

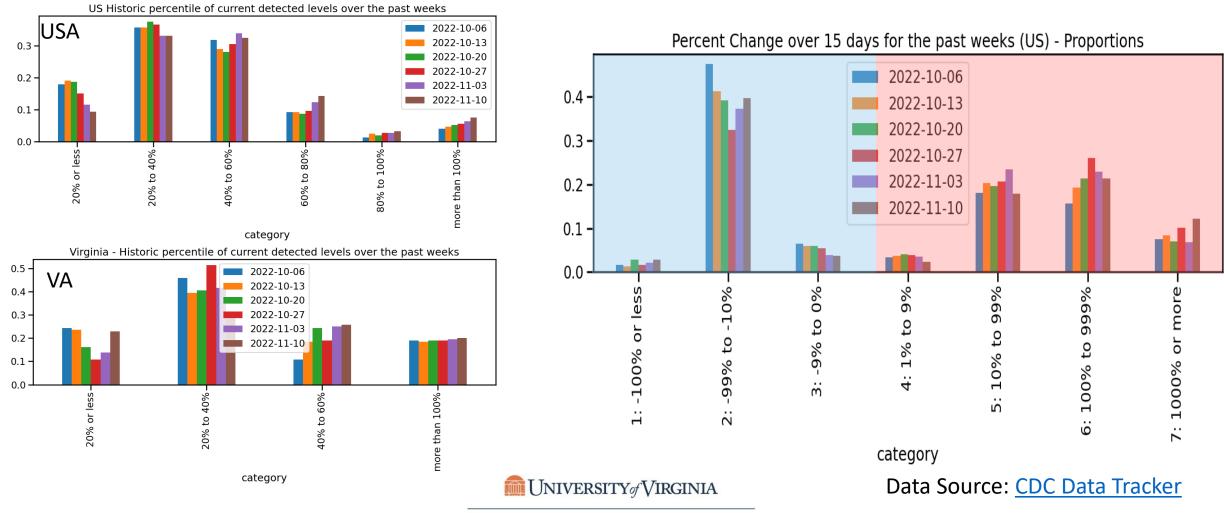


^{1.} Anne Cori, Neil M. Ferguson, Christophe Fraser, Simon Cauchemez. A New Framework and Software to Estimate Time-Varying Reproduction Numbers During Epidemics. American Journal of Epidemiology, Volume 178, Issue 9, 1 November 2013, Pages 1505–1512, https://doi.org/10.1093/aje/kwt133

Wastewater Monitoring

Wastewater provides a coarse early warning of COVID-19 levels in communities

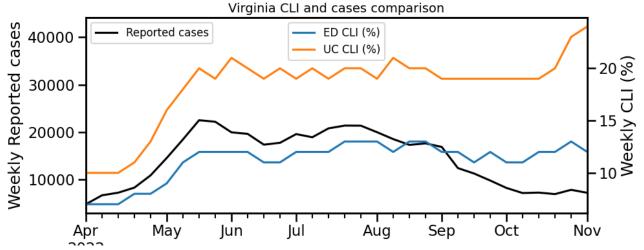
- Overall in the US, there is an increase in sites with increased levels of virus compared to 15 days ago
- Current virus levels are at or exceeding max of previous historical levels, has slowed, though more sites are entering upper quintiles

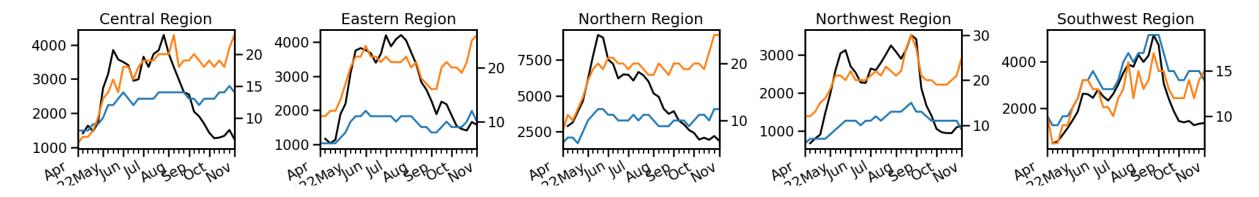


COVID-like Illness Activity

COVID-like Illness (CLI) gives a measure of COVID transmission in the community

- Emergency Dept (ED) based CLI is more correlated with case reporting
- Urgent Care (UC) is a leading indicator but may be influence by testing for other URIs
- After 5 months of plateau UC CLI has experienced 2 weeks of growth to highest level since the initial Omicron waves





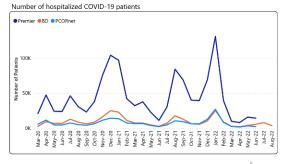


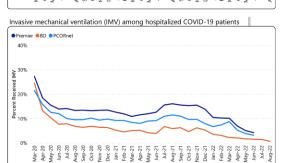
Hospitalizations and Severe Outcomes

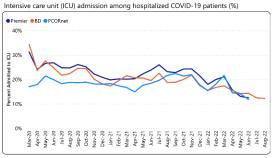
Proportion of most severe outcomes decreasing among those who are hospitalized

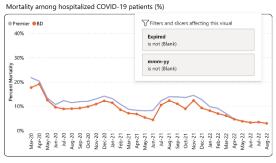
- ICU has declined from ~20% of hospitalized to 10-15% since initial Omicron wave
- Seen across all age-groups
- Recent rises in these rates have subsided in the past week

Data Source: <u>CDC Data Tracker</u>

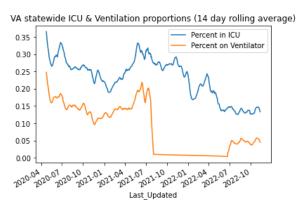




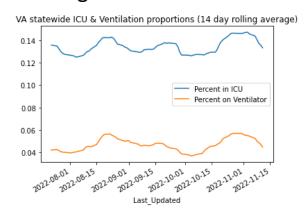




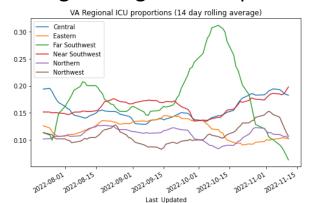
Virginia-wide – full pandemic



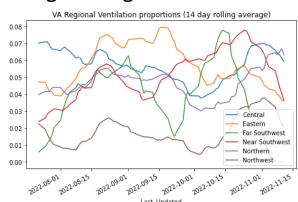
Virginia-wide – recent



Virginia Regional ICU percent



Virginia Regional Ventilation %



18-Nov-22 15

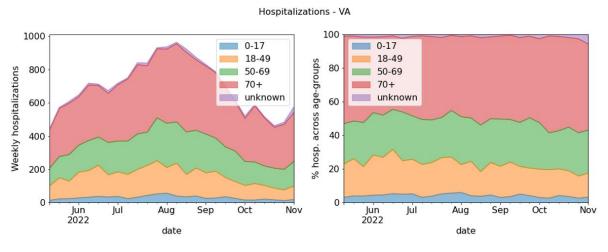
Hospitalizations in VA by Age

Age distribution in hospitals relatively stable

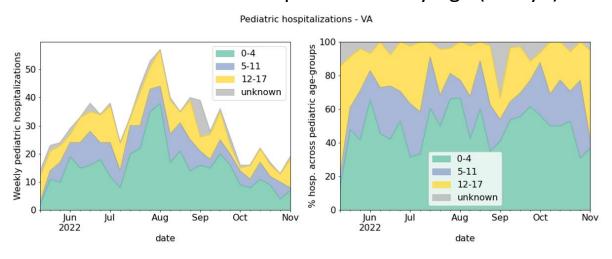
 Recent uptick in overall pediatric hospitalizations, with higher proportion in 12-17 year olds

Note: These data are lagged and based on hospital reporting HHS

Virginia Hospitalizations by Age (all ages)



Pediatric Hospitalizations by Age (0-17yo)

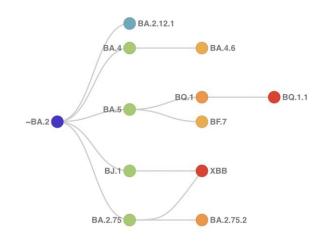


Data Source: <u>Delphi</u> and <u>HHS</u>

SARS-CoV2 Variants of Concern

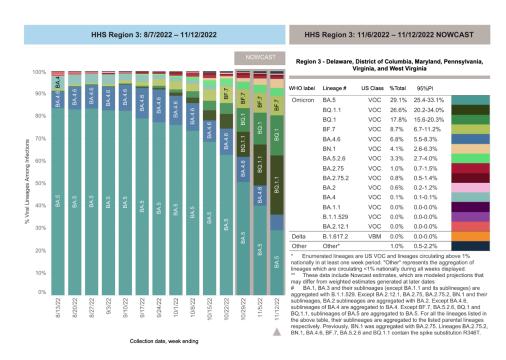
Emerging variants have potential to continue to alter the future trajectories of pandemic and have implications for future control

 Variants have been observed to: increase transmissibility, increase severity (more hospitalizations and/or deaths), and limit immunity provided by prior infection and vaccinations



Omicron Updates

- Soup of tracked variants has grown to 70% from 65% last week
- BQ.1.1 continues to show growth up to 27% from 23%, with BQ.1.* accounting for another 18% up from 14% last week
- BF.7 remains stead at 8.7% and BA.4.6 has shrunk to 7%
- BA.5.2.6 and BN.1 are now broken out by CDC nowcast, and account for relatively smaller shares (3% and 4% respectively)
- BA.2.* account for less than 3% combined
- XBB and subvariants remain a concern

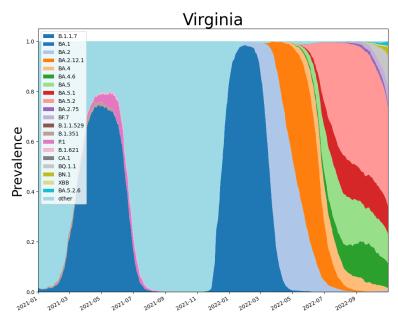


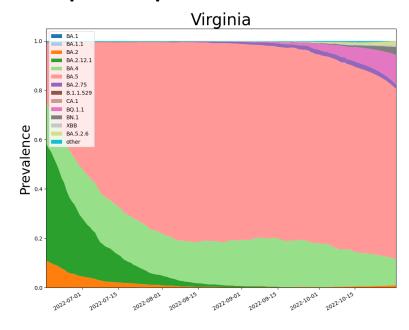
SARS-CoV2 Omicron Sub-Variants



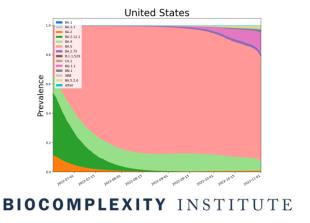
Enabled by data from **GISAID**

As detected in whole Genomes in public repositories

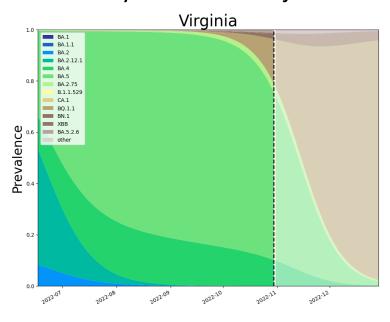


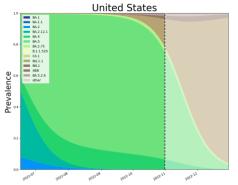


United States United States United States



VoC Polynomial Fit Projections



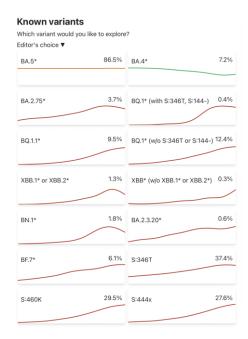


Note: Data lags force projections to start in past. Everything from dotted line forward is a projection.

SARS-CoV2 Omicron Sub-Variants

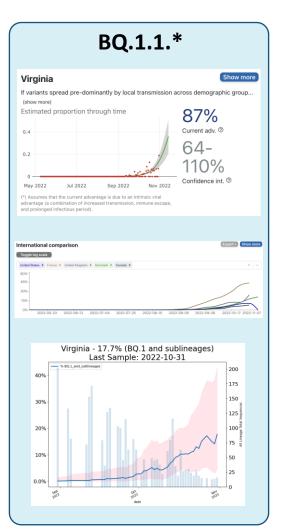
COV-spectrum

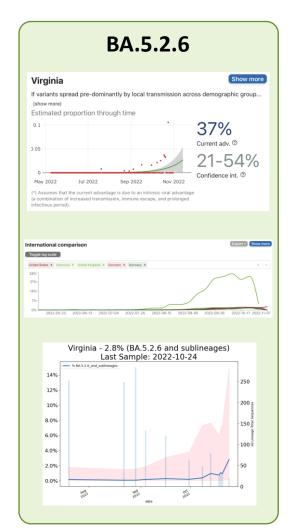
"Editor's choice" Variants to watch

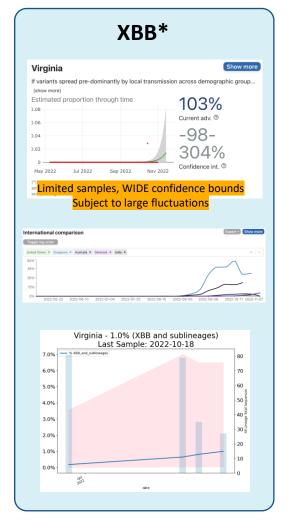




Enabled by data from GISAID



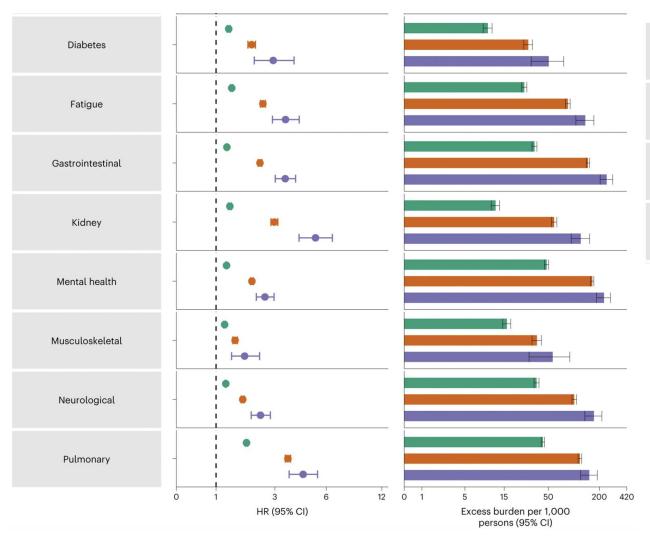


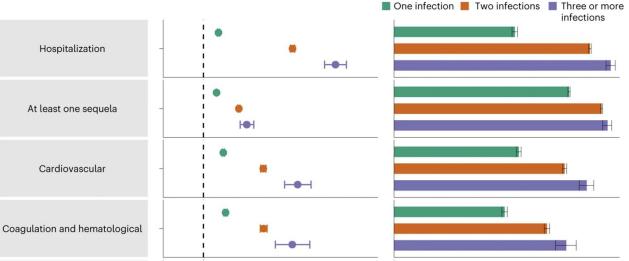




Pandemic Pubs (Nov 15th, 2022)

1. Evidence shows that reinfection further increases risks of death, hospitalization and sequelae in multiple organ systems in the acute and post-acute phase





Researchers used the US Department of Veterans Affairs' national healthcare database to build a cohort of individuals with one SARS-CoV-2 infection (n = 443,588), reinfection (two or more infections, n = 40,947) and a noninfected control (n = 5,334,729). Compared to no reinfection, reinfection contributed additional risks of death (hazard ratio (HR) = 2.17,95% confidence intervals (CI) 1.93-2.45), hospitalization (HR = 3.32,95% CI 3.13-3.51) and sequelae including pulmonary, cardiovascular, hematological, diabetes, gastrointestinal, kidney, mental health, musculoskeletal and neurological disorders.

Researchers selected those still alive 90 d after their first positive SARS-CoV-2 test (n = 489,779) and then further selected participants who experienced reinfection, defined as a positive SARS-CoV-2 test 90 d or more after the first infection, where reinfection could occur between 1 June 2020 and 25 June 2022, which spans the time frame in the US in which pre-Delta, Delta and Omicron variants were dominant.

https://www.nature.com/articles/s41591-022-02051-3#MOESM1

Pandemic Pubs (Nov 15th, 2022)

2. Moderna bivalent elicited a superior neutralizing antibody response against Omicron BA.1 and Omicron BA.4/BA.5 compared to the original booster dose of mRNA-1273

Bivalent BA.5 Booster Neutralizing Antibody Lab Assessments

Lab	Assay	Bivalent vs. BA.5 Compared to Original	Bivalent vs. BQ.1.1 Compared to Original
Moderna	Live virus	5 to 6-fold improved	Increased
Suthar	Live virus	4-fold improved	~10-fold increased (vs 1 booster)
Shi	Live virus	3-fold improved	Low, but 3-fold GMT
Pfizer	Live virus	4-fold improved	Not assessed
Но	Pseudovirus	Minimal difference	Not assessed
Barouch	Pseudovirus	1.3-fold increase	Not assessed
Barouch	Pseudovirus	No difference	Modest ~1.2-fold increase

@erictopol

moderna

Moderna's BA.4/BA.5
Targeting Bivalent Booster,
mRNA-1273.222,
Meets Primary Endpoint of
Superiority Against Omicron
Variants Compared to
Booster Dose of mRNA-1273 in
Phase 2/3 Clinical Trial

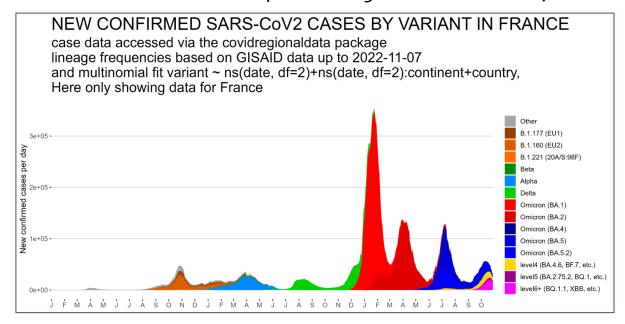
Moderna released updated information indicating (5-6 fold) increase in neutralizing antibodies against BA.5 as compared with the original strain booster. Superiority lasted at least three months. A large assessment of 500 adults showed the increased neutralization. In an exploratory analysis of approximately 40 participants using research assays, both bivalent vaccines demonstrated robust neutralizing activity against BQ.1.1, despite an approximately 5-fold drop in titers compared to BA.4/BA.5.

https://investors.modernatx.com/news/news-details/2022/Modernas-BA.4BA.5-Targeting-Bivalent-Booster-mRNA-1273.222-Meets-Primary-Endpoint-of-Superiority-Against-Omicron-Variants-Compared-to-Booster-Dose-of-mRNA-1273-in-Phase-23-Clinical-Trial/default.aspx

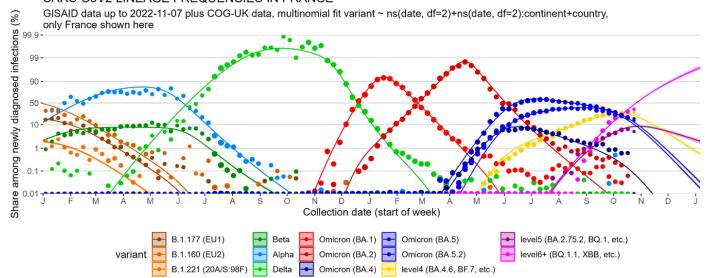
 $\underline{https://erictopol.substack.com/p/new-booster-data-and-variants-galore}$

Pandemic Pubs (Nov 9th, 2022)

1. Trend in France shows positive signs for minimal BQ.1 wave

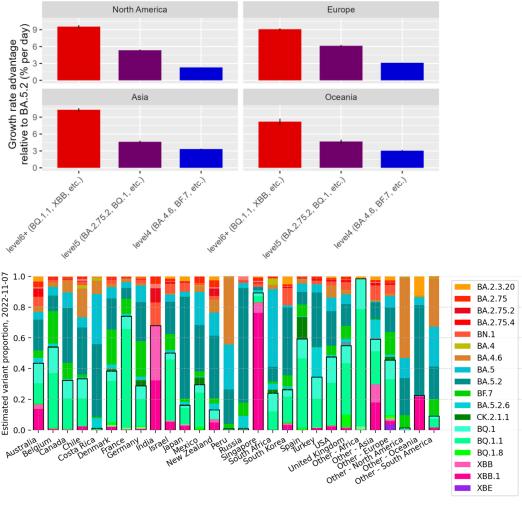


SARS-CoV2 LINEAGE FREQUENCIES IN FRANCE



GROWTH RATE ADVANTAGE OF SARS-CoV2 VARIANTS

based on multinomial fit variant ~ ns(date, df=2)+ns(date, df=2):continent+country GISAID & COG-UK data, using data from countries with >=50 level5 or level6+ variants Estimates shown for continents with >50 sequences of each variant



Tom Wenseleers, professor at KU Leuven and Professor Moritz Gersten at University of Heidelberg estimate a recent reduction in the growth advantage of BQ.1.1 (down to 9-10% over BA.5) and observe a reduction in the new cases confirmed per day. France has been marked as a bellwether relative to the BQ.1.1 variant due to early dominance of the variant there. It remains to be seen if immunity from previous BA.5 wave is the most likely cause of this trend.

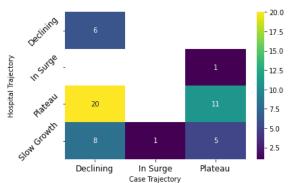
https://twitter.com/TWenseleers/status/1589554986983206913 https://twitter.com/MoritzGerstung/status/1588466692014891008



United States Cases & Hospitalizations



Status	Number of States		
Status	Current Week	Last Week	
Declining	34	(41)	
Plateau	18	(11)	
Slow Growth	1	(2)	
In Surge	1	(0)	



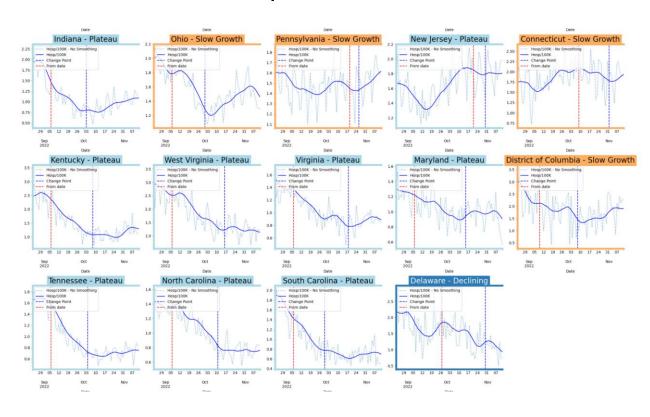
Status	Number of States		
Status	Current Week	Last Week	
Declining	6	(4)	
Plateau	31	(37)	
Slow Growth	14	(11)	
In Surge	2	(1)	

Virginia and Her Neighbors

Cases

2 <= R ■ 1.5 <= R < 2 0.9 <= R < 1.1 0.5 <= R < 0.9 0.2 <= R < 0.5 R < 0.2

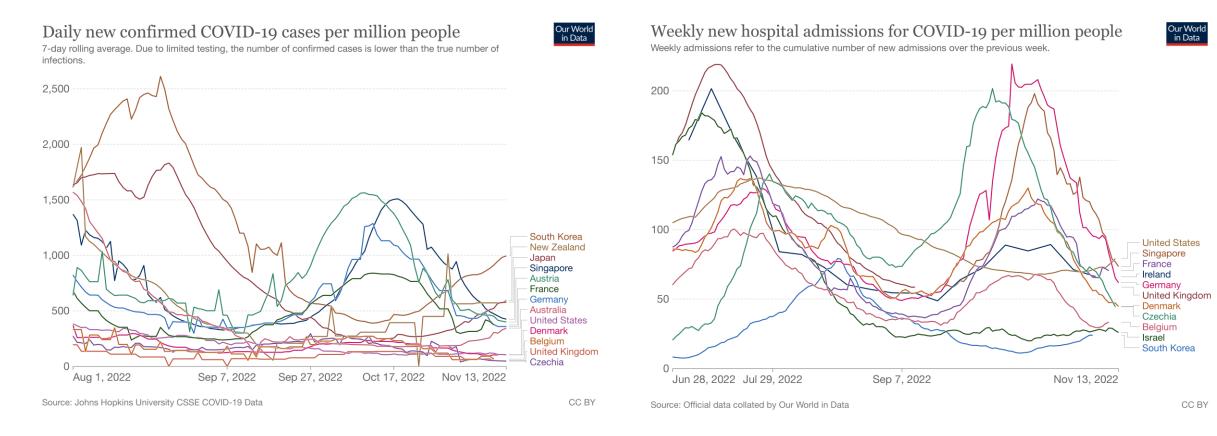
Hospitalizations



Around the World – Various trajectories

Confirmed cases

Hospitalizations





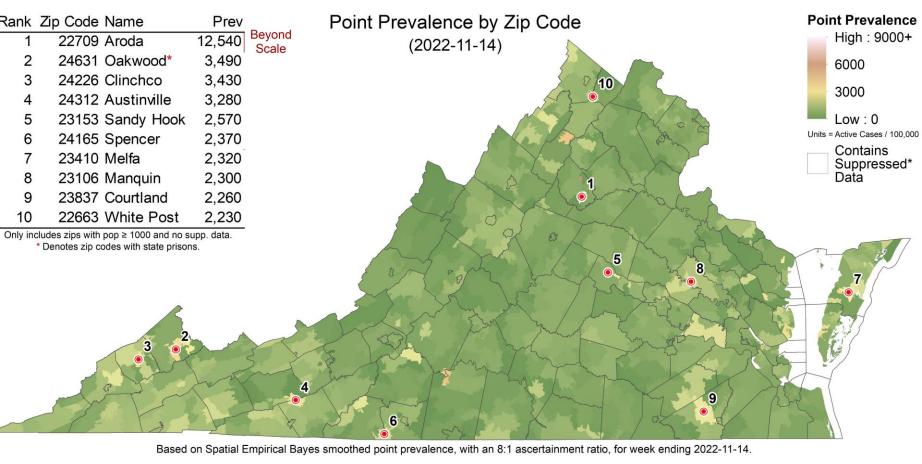
18-Nov-22



Zip code level weekly Case Rate (per 100K)

Case Rates in the last week by zip code

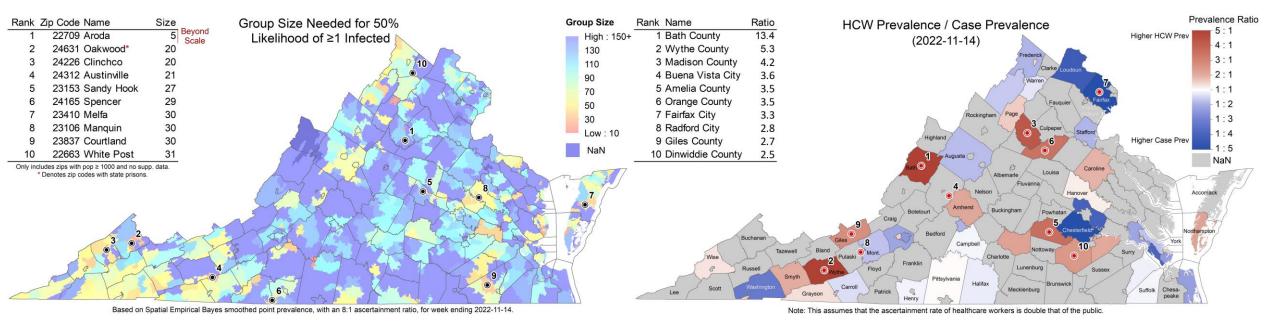
- Statewide rates are low, Rank Zip Code Name with only one zip code reporting an incidence above 3,500 / 100k pp.
- Aroda, VA (in Madison County) is reporting a large spike in cases.
- High prevalence areas are randomly distributed around Virginia. Only one holds a prison.
- Some counts are low and suppressed to protect anonymity. Those are shown with a dark red outline.



Risk of Exposure by Group Size and HCW prevalence

Case Prevalence in the last week by zip code used to calculate risk of encountering someone infected in a gathering of randomly selected people

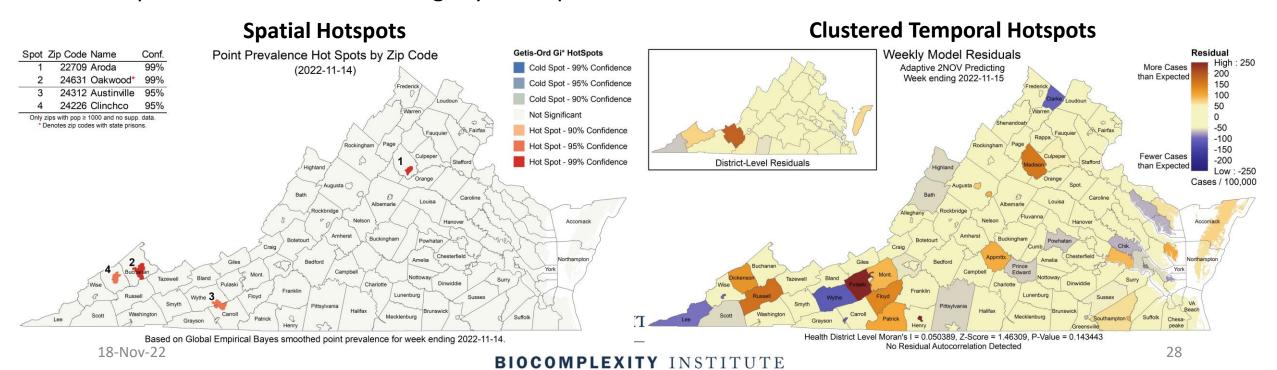
- **Group Size**: Assumes **8 undetected infections** per confirmed case (ascertainment rate from recent seroprevalence survey) and shows minimum size of a group with a 50% chance an individual is infected by zip code (e.g., in a group of 5 in Aroda, there is a 50% chance someone will be infected).
- **HCW ratio**: Case rate among health care workers (HCW) in the last week using patient facing health care workers as the denominator / population's case prevalence. Madison Co. is highlighted (two weeks in a row).



Current Hot-Spots

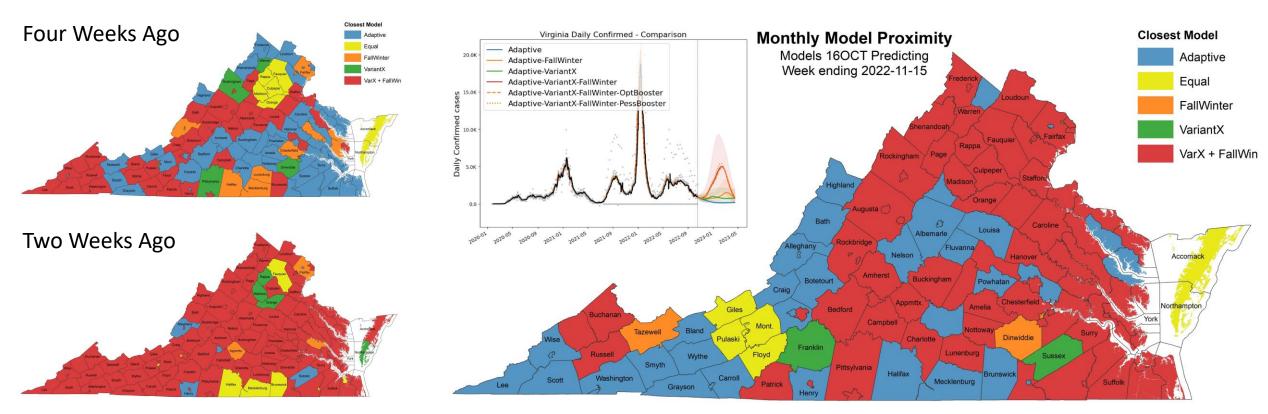
Case rates that are significantly different from neighboring areas or model projections

- Spatial: Getis-Ord Gi* based hot spots compare clusters of zip codes with weekly case prevalence higher than nearby zip codes to identify larger areas with statistically significant deviations
- **Temporal**: The weekly case rate (per 100K) projected last week compared to observed by county, which highlights temporal fluctuations that differ from the model's projections.
- Spatial hotspots are few and sporadic. Temporal hotspots are primarily found west of Roanoke. Models underpredicted New River and slightly underpredicted Cumberland Plateau and Eastern Shore.



Scenario Trajectory Tracking

Which scenario from a month ago did projection for each county track closest?



- One-month projections separate the scenarios more clearly and reveals larger overall patterns.
- Over the last six weeks, the Adaptive scenario has been losing track of the epidemic. The FallWinter-VariantX scenario seemed to track the most counties. This week Adaptive is back in most western counties.

18-Nov-22 29

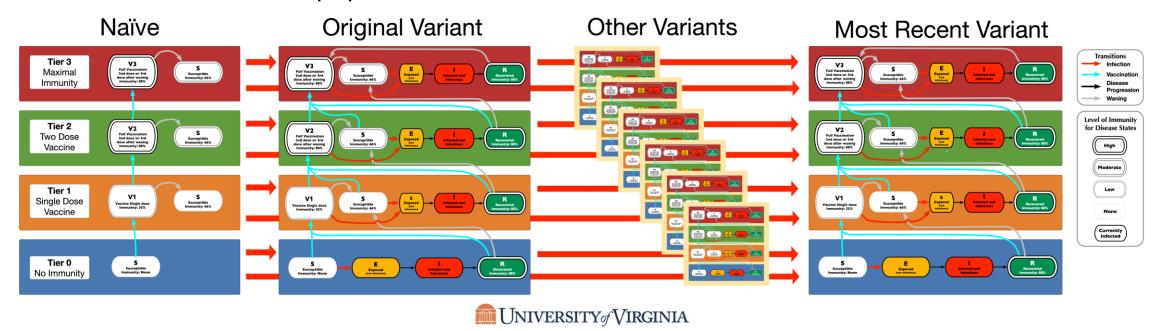
Model Update – Adaptive Fitting



Model Structure Extended for more sub-variants

Omicron sub-variants escape immunity induced by previous sub-variants

- Multiple strain support allows representation of differential protection based on immunological history (BA.1, BA.2, BA.2.12.1, BA.4/5, and future variants (VariantX))
- Each sub-variant has differing levels of immune escape to previous sub-variants, the prevalences are based on observations for fitting purposes, and projections use estimated future prevalences
- Adaptive fitting approach continues to use simulation to generate the full distribution of immune states across the population



Adaptive Fitting Approach

Each county fit precisely, with recent trends used for future projection

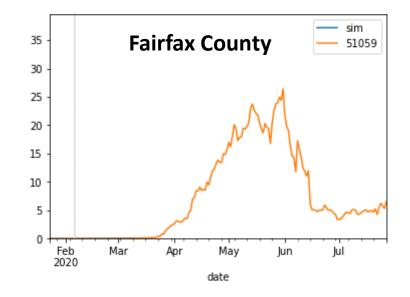
 Allows history to be precisely captured, and used to guide bounds on projections

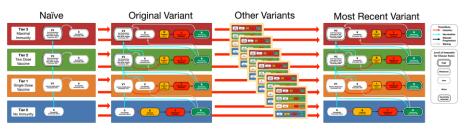
Model: An alternative use of the same meta-population model, PatchSim with multiple tiers of immunity

- Allows for future "what-if" Scenarios to be layered on top of calibrated model
- Allows for waning of immunity and for partial immunity against different outcomes (eg lower protection for infection than death)

External Seeding: Steady low-level importation

 Widespread pandemic eliminates sensitivity to initial conditions, we use steady 1 case per 10M population per day external seeding







Seroprevalence updates to model design

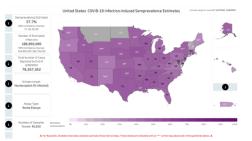
Several seroprevalence studies have stopped

 CDC Nationwide Commercial Laboratory Seroprevalence Survey is no longer reporting updates; pre-Omicron this data estimated ascertainment ratio of ~4-6x

Testing Behavior has changed, fewer cases are reported

- Home testing, reduced symptoms due to breakthrough / reinfection, and elimination of public health leave
- Outbreaks Near Me from Boston Children's Hospital and Momentive collects reports of home testing
- Wastewater data is consistent with case ascertainment being significantly lower than during the Omicron BA.1 wave
- Accounting for home testing, changes case ascertainment to be 2 times more than pre-Omicron resulting in a current rate of 16 infections to one case

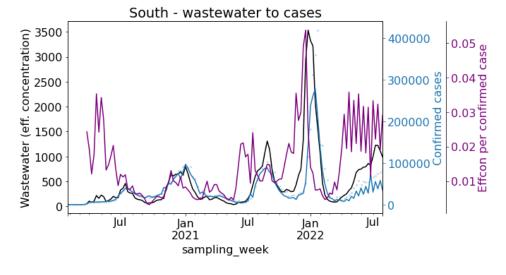




Virginia

Feb 22nd: 45% [42% - 48%]; Jan 22nd: 34% [31%-39%]

https://covid.cdc.gov/covid-data-tracker/#national-lab





Calibration Approach

- Data:
 - County level case counts by date of onset (from VDH)
 - Confirmed cases for model fitting
- **Calibration:** fit model to observed data and ensemble's forecast
 - Tune transmissibility across ranges of:
 - Duration of incubation (5-9 days), infectiousness (3-7 days)
 - Undocumented case rate (1x to 7x) guided by seroprevalence studies
 - Detection delay: exposure to confirmation (4-12 days)
 - Approach captures uncertainty, but allows model to precisely track the full trajectory of the outbreak
- **Project:** future cases and outcomes generated using the collection of fit models run into the future
 - Mean trend from last 7 days of observed cases and first week of ensemble's forecast used
 - Outliers removed based on variances in the previous 3 weeks
 - 2 week interpolation to smooth transitions in rapidly changing trajectories
- **Outcomes**: Data driven by shift and ratio that has least error in last month of observations
 - Hospitalizations: 3 days from confirmation, 6.8% of cases hospitalized
 - Deaths: 11 days from confirmation, 1.45% of cases die





COVID-19 in Virginia: Summary



Dashboard Updated: 11/16/2022 Data entered by 5:00 PM the prior day.

Cases, Hospitalizations and Deaths

Total Cases* 2,135,778 **Total Hospital** Admissions**

Total Deaths

(New Cases: 988)

57.287

22,253

1.508.385

627,393

Confirmed[†] 53.735

3.552

Confirmed[†] 18.466

3.787

- * Includes both people with a positive test (Confirmed), and symptomatic with a known exposure to COVID-19 (Probable).
- ** Hospitalization of a case is captured at the time VDH performs case investigation. This underrepresents the total number of hospitalizations in
- ^New cases represent the number of confirmed and probable cases reported to VDH in the past 24 hours.
- † VDH adopted the updated CDC COVID-19 confirmed and probable surveillance case definitions on September 1st, 2021. Found here: https://ndc.services.cdc.gov/case-definitions/coronavirus-disease-2019-2021/

Source: Cases - Virginia Electronic Disease Surveillance System (VEDSS), data entered by 5:00 PM the prior day.

Outbreaks

Total Outbreaks*

Outbreak Associated Cases

10.157

166,692

* At least two (2) lab confirmed cases are required to classify an outbreak.

Testing (PCR Only)

Testing Encounters PCR Only*

Current 7-Day Positivity Rate PCR Only**

15,376,572

7.4%

- * PCR" refers to "Reverse transcriptase polymerase chain reaction laboratory testing."
- ** Lab reports may not have been received yet. Percent positivity is not calculated for days with incomplete data

Multisystem Inflammatory
Syndrome in Children

Total Cases*

Total Deaths

180

*Cases defined by CDC HAN case definition: https://emergency.cdc.gov/han/2020/han00432.asp

Accessed 9:45am November 16, 2022

https://www.vdh.virginia.gov/coronavirus/



Scenarios – Transmission Conditions

- Variety of factors continue to drive transmission rates
 - Seasonal impact of weather patterns, travel and gatherings, fatigue and premature relaxation of infection control practices
- Waning Immunity: Omicron waning with a mean of 4 months
- Projection Condition Ingredients:
 - Adaptive: Controls remain as currently experienced into the future with NO influence from other conditions (eg seasonal, variants, etc.)
 - Seasonal (Fall-Winter boosting): Controls remain the same, however, seasonal forcing similar to past Fall-Winter waves is added from Sept-Feb
 - Vaccine Booster Campaign (Booster): Reformulated booster available this fall provides improved immunity against Omicron sub-variants
 - New Variants (VariantX): As of yet unidentified novel sub-variant with similar immune escape but no transmission advantage emerges 4 months after the last significant sub-variant and grows at a similar rate



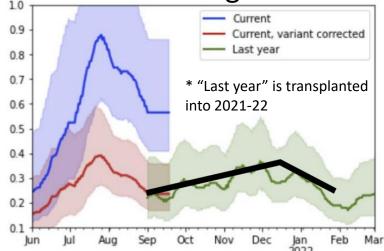
Scenarios – FallWinter

September – February saw strong waves of transmission for both years

- Based on analyses of the past 2 seasons we generate a "coarse baseline transmission boost"
 - In 2021 the distribution of fitted model transmissibility was nearly identical between these periods when corrected for Delta's increased transmissibility

• FallWinter captures these "transmission drivers" from the past and uses them as if they

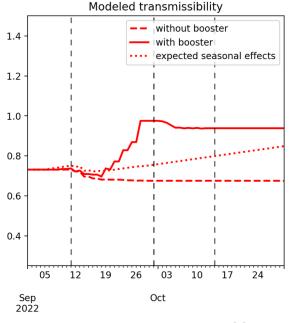
were to occur again this season



Fitting: Black line represents the coarsely fitted base transmissibility

2022 FallWinter is likely different:

With the current level of boosting the transmissibility needs to be much higher to maintain the same amount of cases. The dotted line shows what transmission levels are needed to fit cases without booster and with seasonal effects.



Scenarios – Optimistic vs. Pessimistic Booster Coverage

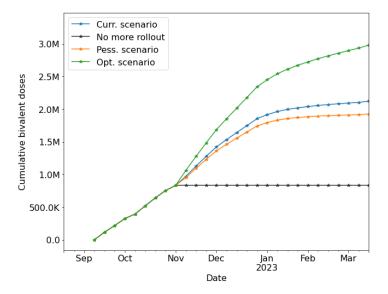
Reformulated Boosters available now

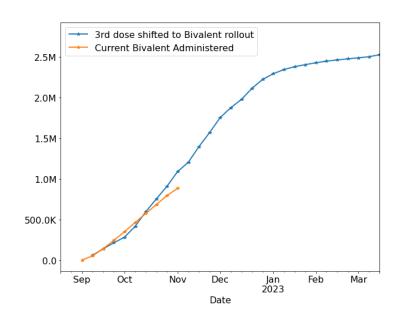
- Assuming Vax efficacy for BA.4/5 and previous variants is 80% against symptomatic illness
- Campaign follows current ground truth to present
- Variant X has same immune escape to these vaccines as against BA.5 (33%)

Current pace: Follows 3rd dose rollout, but maintains current pace relative to it (eg if slower, same slower rate continues into future)

Optimistic pace: 25% higher than previous 3rd dose schedule

No More: No further Bivalent boosters administered





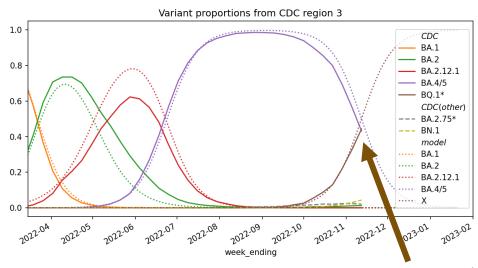
18-Nov-22

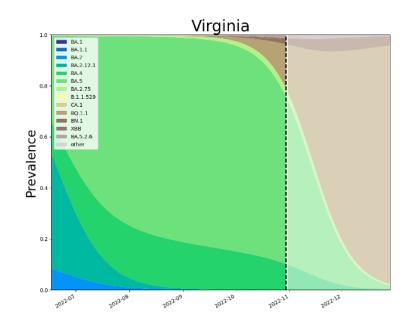
Scenarios – Variant X

Omicron sub-variants seem to be emerging and then dominating with some regularity

- An increasingly complex soup of variants with demonstrated growth advantages in other countries and states continues to grow
- BQ.1.1, XBB, and others have shown evidence of significant immune escape, BQ.1.1 currently growing quickly in US and VA, it remains possible that several may simultaneously expand
- VariantX represents the next variant or the potential swarm of several. We assumes similar growth and level of immune escape against previous sub-variants as BA.4/5 (same transmissibility and 30% immune escape against BA.4/5, higher for other sub-variants).

Sub-Variants with Fitted Prevalences and Hypothetical Future waves





Variant X reaches 50% on Nov 12th

Projection Scenarios – Combined Conditions

Name	Txm	Variant	Booster	Description
Adaptive	С	SQ	Current	Likely trajectory based on conditions remaining similar to the current experience, includes immune escape due to Omicron
Adaptive-FallWinter	FallWinter	SQ	Current	Like Adaptive, with seasonal forcing of FallWinter added on
Adaptive-VariantX	С	X	Current	Like Adaptive, with emergence of a speculative unknown variant 4 months after BA.4/5 with similar level of immune escape and equal transmissibility
Adaptive-VariantX-FallWinter	FallWinter	X	Current	Like Adaptive-VariantX but with the seasonal force of FallWinter added on
Adaptive-VariantX-FallWinter- OptBooster	FallWinter	X	Optimistic	Like Adaptive-VariantX-Fall Winter but with Optimistic Booster (25% more than 3 rd dose rollout)
Adaptive-VariantX-FallWinter- NoMoreBooster	FallWinter	X	No More	Like Adaptive-VariantX-FallWinter but with no additional Booster doses

Transmission: C = Current levels persist into the future

FallWinter = Transmission rates learned from Sept through February of past seasons are estimated and

added as a seasonal boosting to baseline transmission rates

Variant: SQ = Status quo prevalences remaint the same (e.g. no significant major driving of transmission anticipated)

X = Novel sub-variant scenario, new variant emerges reaches dominance in near term, 30% immune escape

Booster: Current = Current pace relative to 3rd dose rollout is maintained in the future

Optimistic = Starting this week, additional 25% over the 3rd dose rollout is maintained into the future

No More = Starting this week, no additional doses of the booster are administered

Model Results

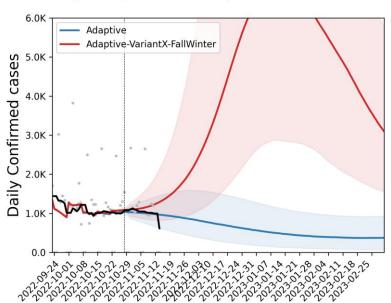


Previous projections comparison - Cases

- Previous projections continue to track observed cases
- Projection from 2 weeks ago projected plateau a week after cases started to plateau
- Projection from 4 weeks ago projected slower decline better capturing recent slowing
- Projection from early July remains eerily on track

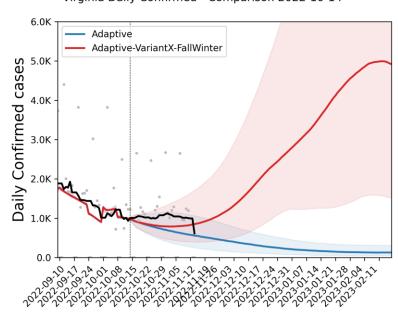
Previous round (2 weeks ago)

Virginia Daily Confirmed - Comparison 2022-10-28



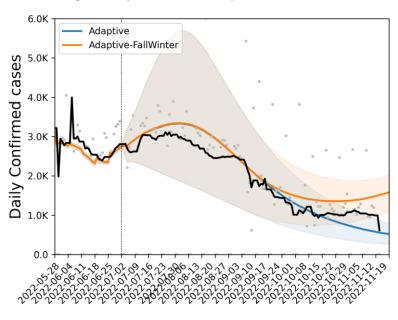
Projection from 4 weeks ago

Virginia Daily Confirmed - Comparison 2022-10-14



Projection from 3 months ago

Virginia Daily Confirmed - Comparison 2022-07-02



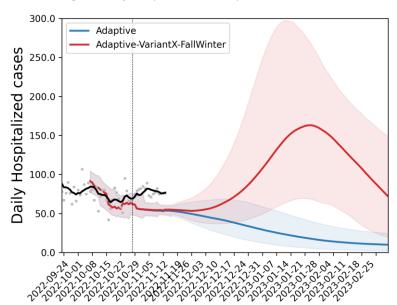
18-Nov-22 41

Previous projections comparison - Hospitalizations

- Previous projections have tracked observed hospitalizations well
- Projection from 2 weeks ago projected continued decline, missed bump
- Projection from early July anticipated a plateau has tracked reasonably well up to present

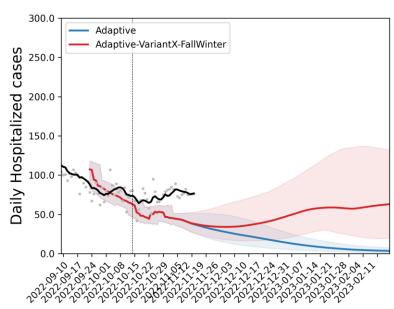
Previous round (2 weeks ago)

Virginia Daily Hospitalized - Comparison 2022-10-28



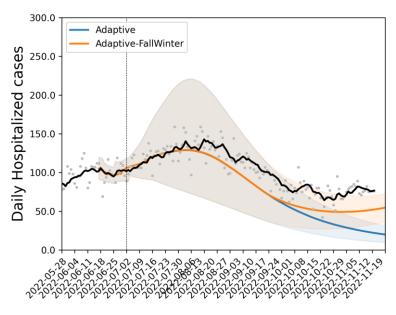
Projection from 4 weeks ago

Virginia Daily Hospitalized - Comparison 2022-10-14



Projection from 3 months ago

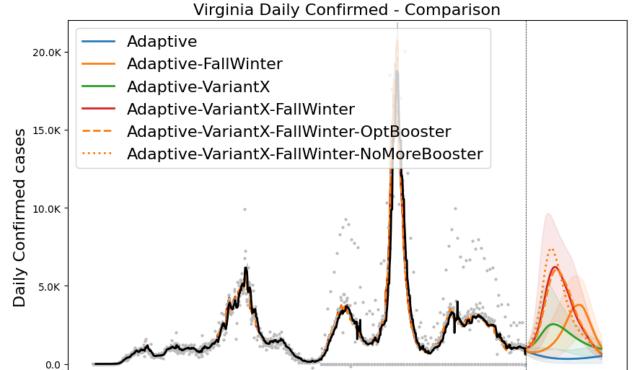
Virginia Daily Hospitalized - Comparison 2022-07-02



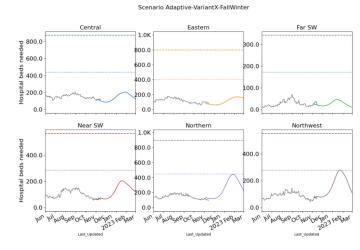
18-Nov-22 42

Outcome Projections

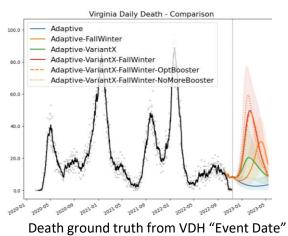
Confirmed cases



Estimated Hospital Occupancy

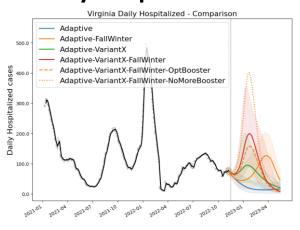


Daily Deaths



Death ground truth from VDH "Event Date" data, most recent dates are not complete

Daily Hospitalized



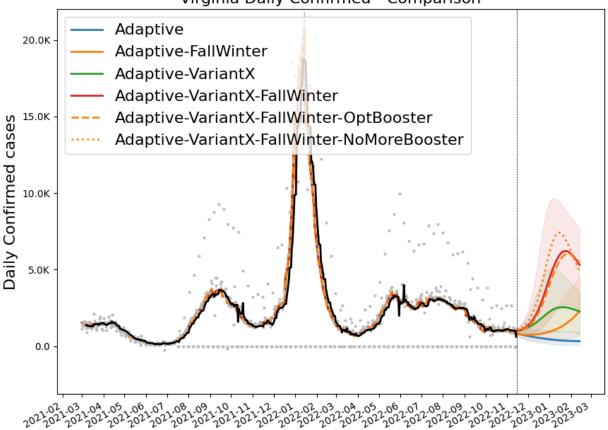
^{*} without surveillance correction VariantBA2 peaked over 10K in July



Outcome Projections – Closer Look

Confirmed cases

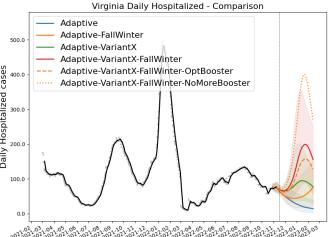




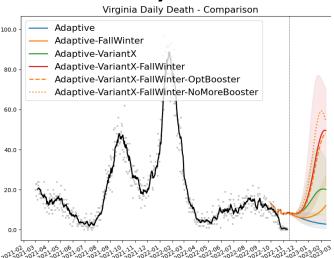
* without surveillance correction VariantBA2 peaked over 10K in July

UNIVERSITY OF VIRGINIA BIOCOMPLEXITY INSTITUTE

Daily Hospitalized



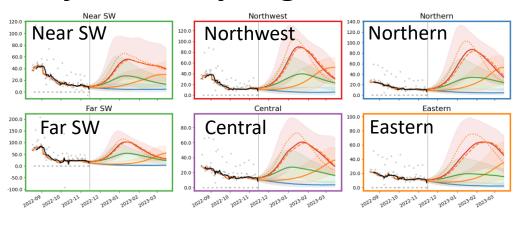
Daily Deaths



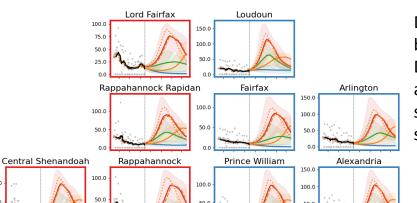
Death ground truth from VDH "Event Date" data, most recent dates are not complete

Detailed Projections: Cases for All Scenarios

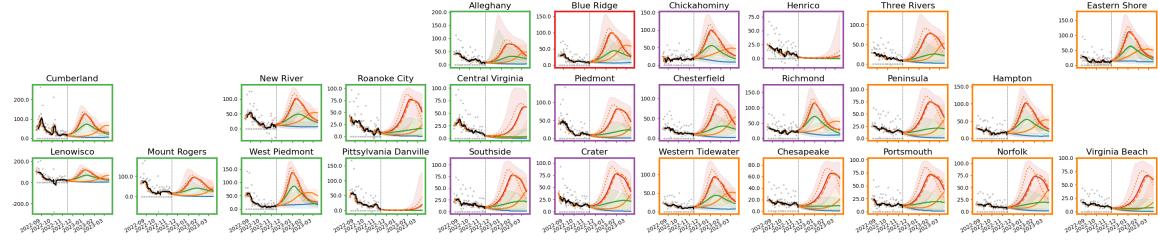
Projections by Region



Projections by District



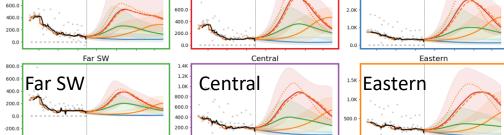
Daily confirmed cases) by rate (per 100K) District (grey with 7-day average in black) with simulation colored by scenario



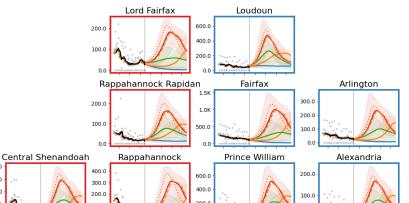
Detailed Projections: Cases for All Scenarios - Closer Look

Projections by Region

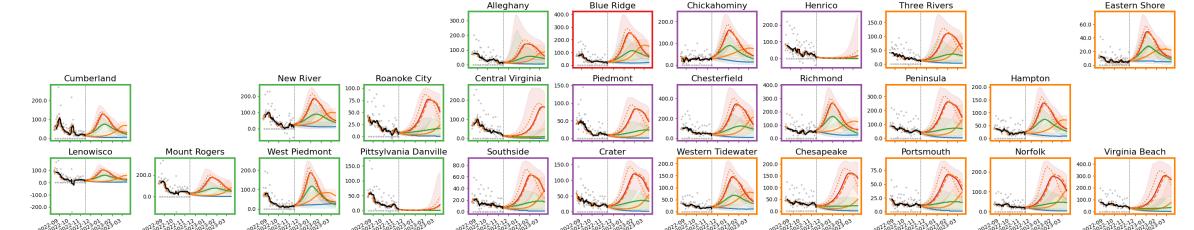
Near SW Northwest Northern Near SW Northwest Northern Northern



Projections by District

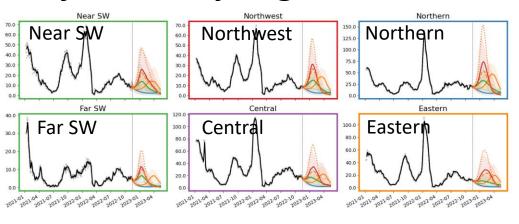


Daily confirmed cases by rate (per 100K) District (grey with 7-day average in black) with simulation colored by scenario

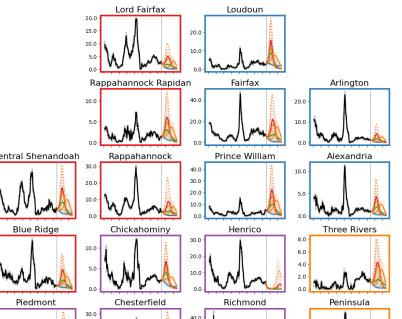


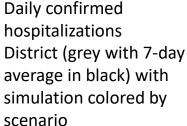
Detailed Projections: Hospitalizations for All Scenarios

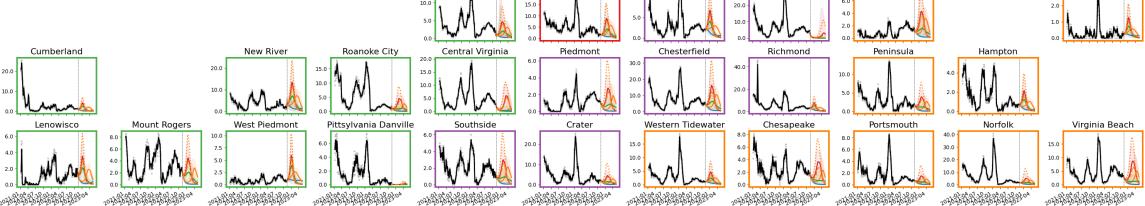
Projections by Region



Projections by District







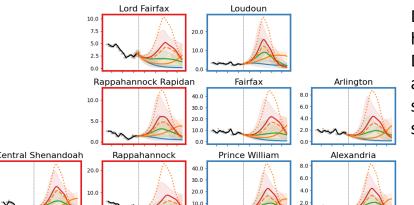
Eastern Shore

Detailed Projections: Hosps for All Scenarios - Closer Look

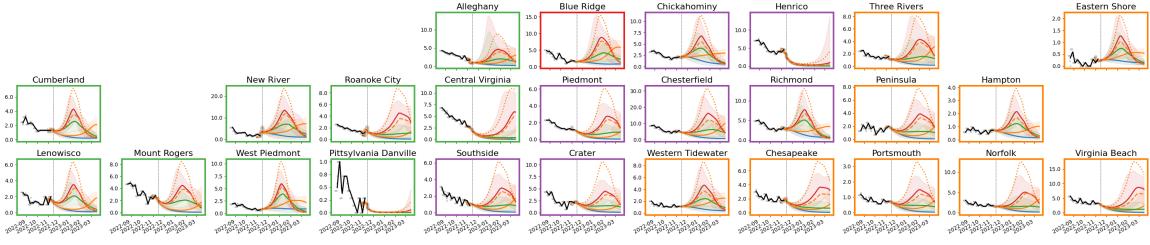
Projections by Region

Near SW Northwest Northern So.0 Northern So.0 Northern So.0 So.0

Projections by District



Daily confirmed hospitalizations District (grey with 7-day average in black) with simulation colored by scenario



Cases Per 100K

0-50

51-100

101-150

251-300

301-350

351-400

401+

Cases Per 100K

0-50

51-100

101-150

151-200

251-300

301-350

351-400

401+

201-250

151-200

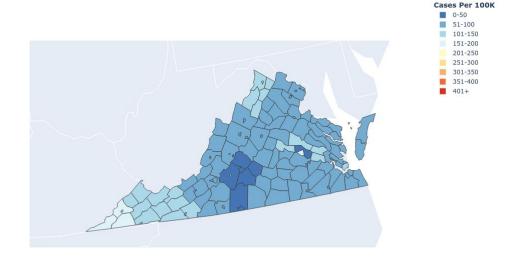
201-250

Impact of Optimistic vs. Pessimistic Booster Distribution

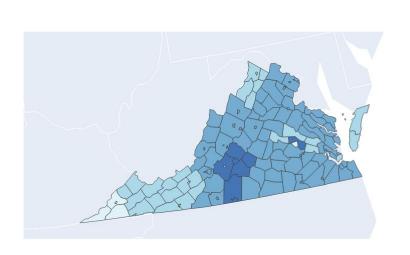
0-50 51-100 101-150 151-200

201-250 251-300 301-350 351-400

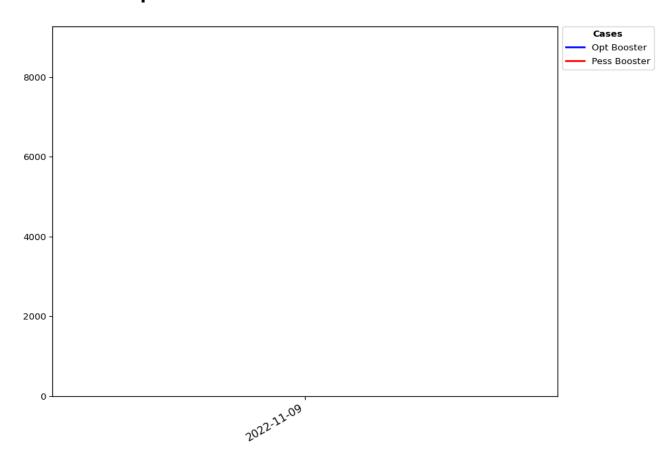
Weekly Projections (Optimistic Booster) 09-Nov-2022



Weekly Projections (Pessimistic Booster) 09-Nov-2022



Cases for Optimistic vs. Pessimistic Boosters 09-Nov-2022

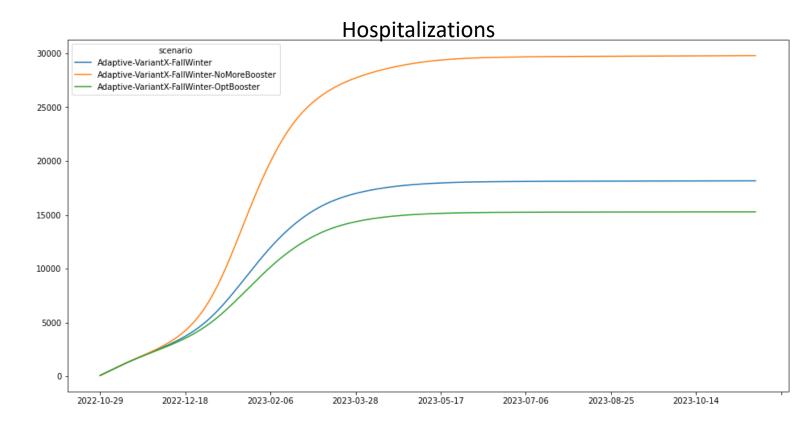


Booster Campaign Coverage has impact on future hospitalizations

Booster Campaign can significantly limit future hospitalizations and severe outcomes

- Optimistic scenario (higher coverage) shows potential to avert ~3000 additional hospitalizations
- No More Booster scenario shows additional ~12K hospitalizations without any future bivalent booster administrations

This is despite a VariantX emerging that has demonstrated immune escape (30%) against the bivalent booster in near term



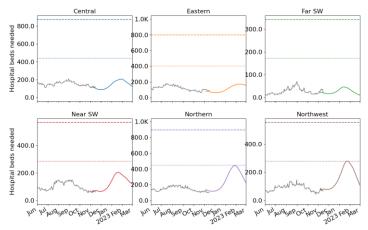


Hospital Demand and Bed Capacity by Region

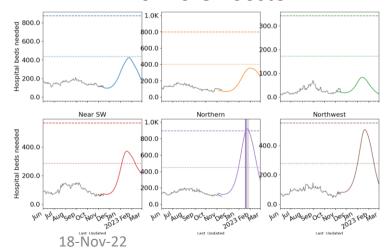
Capacities by Region

COVID-19 capacity ranges from 80% (dots) to 120% (dash) of total beds

Adaptive – VariantX & Fall Winter



Adaptive – VariantX & Fall Winter No More Booster



Length of Stay more variable with Omicron, occupancy projections may vary as a result, ad-hoc estimation performed per region

Length of S	tay Estimates
-------------	---------------

Central	6
Eastern	6
Far SW	4
Near SW	9
Northern	5
Northwestern	9

Estimated LOS shortened slightly to better fit observed data

Projections show continued declines and with expanded capacities and adjusted length of stay, no capacities exceeded





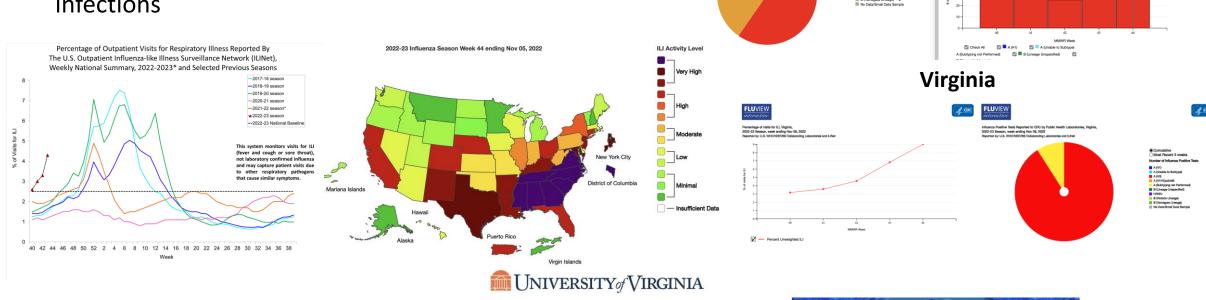
Influenza Update



Current Influenza Situation — ILI Activity

Influenza Activity is Higher than Usual

- Virginia at "Very High" activity along with most of the Southeast, with "High" activity shifting out across US
- Moved from 7% of visits for ILI to 9% this week.
- National ILI activity at highest point in mid-Nov since 2009 pandemic which had large spike in early October
- After starting with high proportions of H3N2 typed influenza, H1N1pdm09 now represents ~1/3 of all infections



BIOCOMPLEXITY INSTITUTE

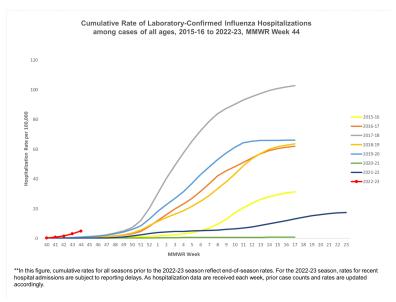
Region 3

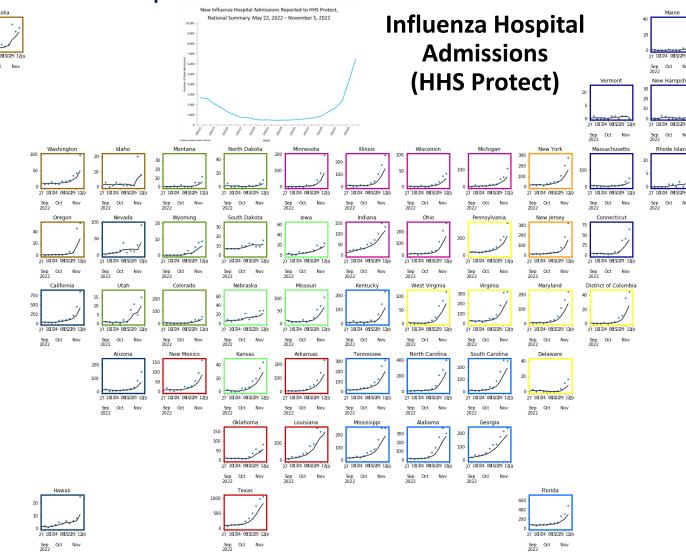
■ STACKED COLUMN CHART WHO/NREVSS

Current Influenza Situation - Hospitalizations

Influenza A hospitalizations continues rapid growth

- National level of influenza hospitalizations
- Nearly all states have doubled their hospitalizations due to influenza in the last couple weeks
- Virginia shows leveling off in the last week







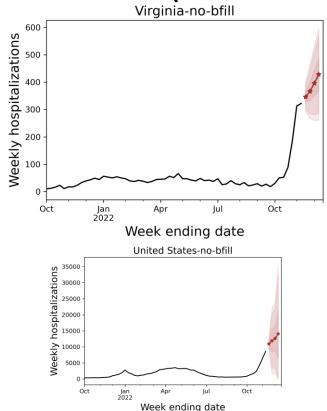


Current Influenza Hospitalization Forecast

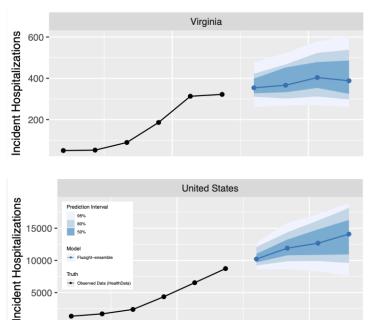
Statistical models for submitting to CDC FluSight forecasting challenge

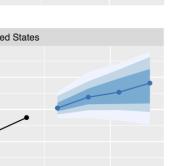
• Similar to COVID-19 case forecasts, uses a variety of statistical and ML approaches to forecast weekly hospital admissions for the next 4 weeks for all states in the US

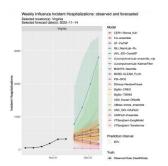
Hospital Admissions for Influenza and Forecast for next 4 weeks (UVA ensemble)

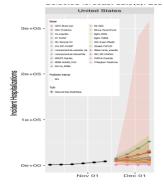


Hospital Admissions for Influenza and Forecast for next 4 weeks (CDC FluSight Ensemble)









Some individual models forecast rapid rises in VA



15000

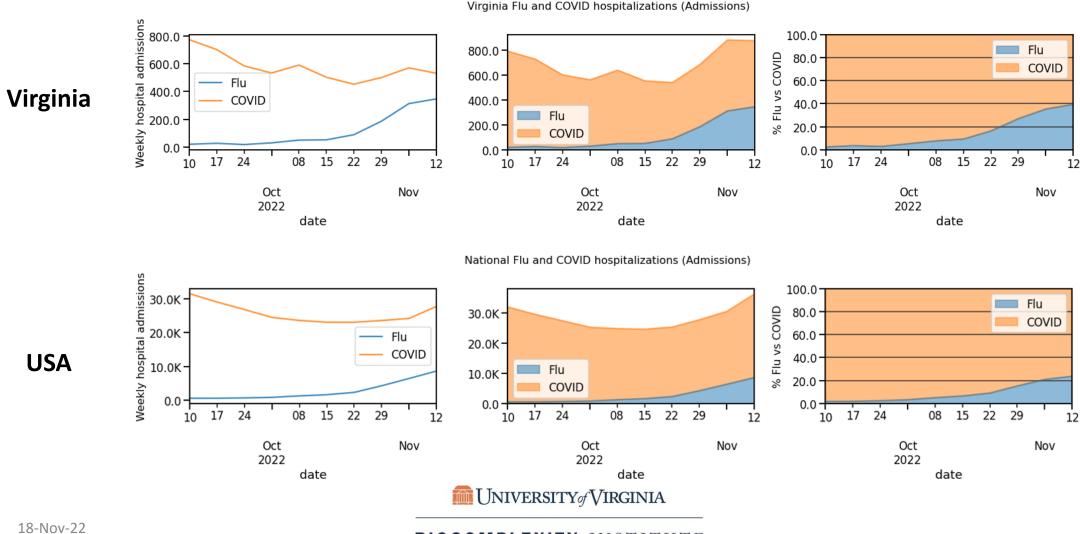
10000

5000



Current Combined Hospitalizations (COVID-19 & Influenza)

COVID-19 and Influenza Weekly Hospitalizations (HHS Protect)



Combined ILI and COVID-19 Hospitalizations

Ensemble methodology that combines the Adaptive with machine learning and statistical models such as:

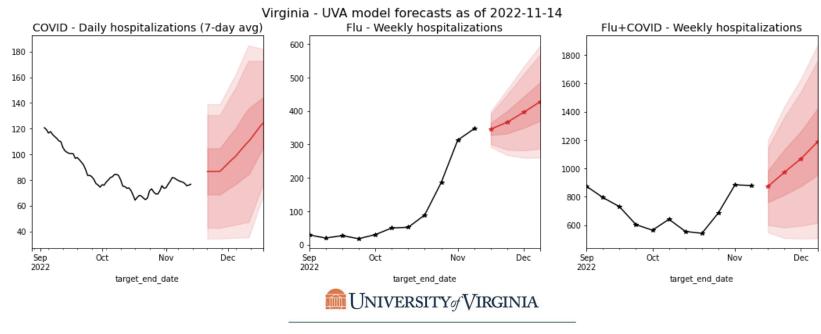
• Autoregressive (AR, ARIMA), Neural networks (LSTM), Kalman filtering (EnKF), G-model (phase), Holt-Winters

Weekly forecasts of hospitalizations done at state level.

Models chosen because of their track record in disease forecasting and to increase diversity and robustness.

Both are regularly submitted to CDC Forecast Hubs

Weekly Hospitalizations Short-term COVID-19 and Influenza Forecasts



Scenario Modeling Hub - COVID-19 and Influenza

Collaboration of multiple academic teams to provide national and state-by-state level projections for 4 aligned scenarios

COVID-19 Scenarios

- Scenario A
 Early boosters
 No new variant
 (A-2022-07-19)
- Scenario C
 Late boosters
 No new variant
 (C-2022-07-19)
- Scenario B
 Early boosters
 New immune escape
 variant
 (B-2022-07-19)
- Scenario D
 Late boosters
 New immune escape
 variant
 (D-2022-07-19)

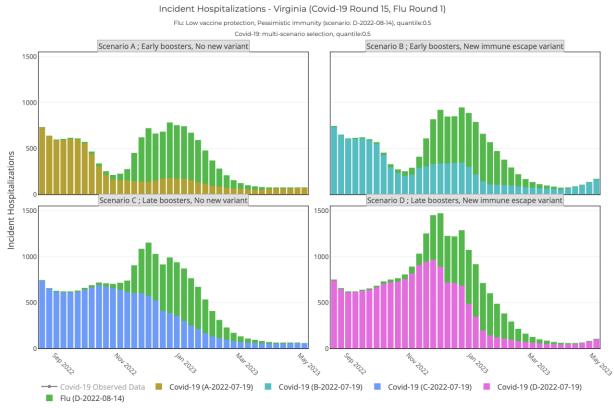
Influenza Scenarios

- O High vaccine protection, Optimistic immunity (A-2022-08-14)
- High vaccine protection, Pessimistic immunity (B-2022-08-14)
- O Low vaccine protection, Optimistic immunity (C-2022-08-14)
- Low vaccine protection, Pessimistic immunity (D-2022-08-14)

Round 16 of COVID-19 in progress, Round 2 of Influenza in planning stages; should be available by Thanksgiving

Combined Hospitalizations (VA)

Interactive visualization – MultiPathogen Plot https://covid19scenariomodelinghub.org/viz.html



COVID -19 scenarios and most "pessimistic" influenza scenarios combined

Scenario Modeling Hub - COVID-19 (Round 15)

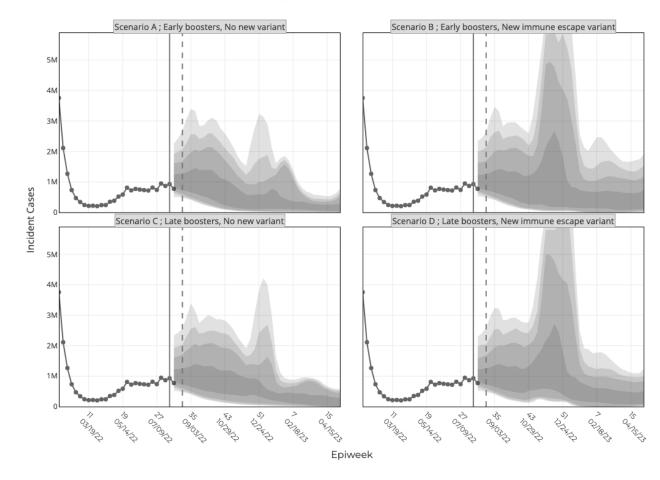
Collaboration of multiple academic teams to provide national and state-by-state level projections for 4 aligned scenarios

- Round 15 results published
 - Scenarios: Test benefits of reformulated fall boosters w/ and w/out a new variant
 - Timing of reformulated boosters is one of the axes

Round 16 in progress stages should be available by mid/late-November

https://covid19scenariomodelinghub.org/viz.html

Projected Incident Cases by Epidemiological Week and by Scenario for Round 15 - US (- Projection Epiweek; -- Current Week)



18-Nov-22

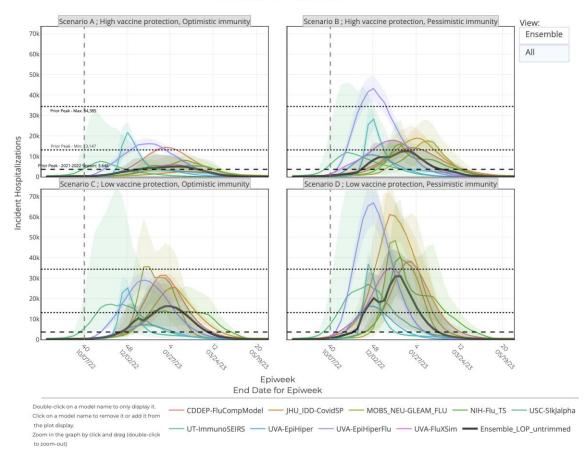
Scenario Modeling Hub – Influenza (Round 1)

Collaboration of multiple academic teams to provide national and state-by-state level projections for 4 aligned scenarios

- Round 1 results recently published
 - Impact of missed flu seasons on preseason immunity
 - Testing different seasonal vaccine coverage and efficacy
 - Projected from Aug 14th 2022
- High degree of uncertainty as previous 2 seasons have been irregular and there is still limited data for this season available
- Demonstrates importance of good vaccine coverage especially if previous immunity is weak

https://fluscenariomodelinghub.org/viz.html

Projected Incident Hospitalizations by Epidemiological Week and by Scenario for Round 1 - US (-Projection Epiweek; -- Current Week)



18-Nov-22 61

Key Takeaways

Projecting future cases precisely is impossible and unnecessary. Even without perfect projections, we can confidently draw conclusions:

- Case rates and hospitalizations remain relatively flat
- VA weekly case rate is down to 72/100K from 81/100K (potential surveillance artifacts)
 - US weekly case rate is flat remaining at 73 per 100K from 74 per 100K
- VA hospital occupancy is slightly down (rolling 7 day mean of 478 from 482 a week ago) though admissions are up
 - Influenza hospitalization shows an increase in admissions though growth has stalled, however, with over 300 hospitalizations in the last week
- Projections anticipate increases in cases and hospitalizations in coming weeks
 - Combined Hospitalizations due to Influenza and COVID-19 expected to increase in short-term
- Model updates:
 - Variant X candidates have now reached 50% (BQ.1.1, BN.1, BF.7 and others and XBB among others), 50% remains at Nov 12th
 - Modified Booster Scenarios: Current pace (included in all scenarios) with comparisons between Optimistic rollout and a more Pessimistic scenario where vaccination halts at current levels

The situation continues to change. Models continue to be updated regularly.

18-Nov-22 62

References

Venkatramanan, S., et al. "Optimizing spatial allocation of seasonal influenza vaccine under temporal constraints." *PLoS Computational Biology* 15.9 (2019): e1007111.

Arindam Fadikar, Dave Higdon, Jiangzhuo Chen, Bryan Lewis, Srinivasan Venkatramanan, and Madhav Marathe. Calibrating a stochastic, agent-based model using quantile-based emulation. SIAM/ASA Journal on Uncertainty Quantification, 6(4):1685–1706, 2018.

Adiga, Aniruddha, Srinivasan Venkatramanan, Akhil Peddireddy, et al. "Evaluating the impact of international airline suspensions on COVID-19 direct importation risk." *medRxiv* (2020)

NSSAC. PatchSim: Code for simulating the metapopulation SEIR model. https://github.com/NSSAC/PatchSim

Virginia Department of Health. COVID-19 in Virginia. http://www.vdh.virginia.gov/coronavirus/

Biocomplexity Institute. COVID-19 Surveillance Dashboard. https://nssac.bii.virginia.edu/covid-19/dashboard/

Google. COVID-19 community mobility reports. https://www.google.com/covid19/mobility/

Biocomplexity page for data and other resources related to COVID-19: https://covid19.biocomplexity.virginia.edu/



Questions?

Points of Contact

Bryan Lewis brylew@virginia.edu

Srini Venkatramanan srini@virginia.edu

Madhav Marathe marathe@virginia.edu

Chris Barrett@virginia.edu

Biocomplexity COVID-19 Response Team

Aniruddha Adiga, Abhijin Adiga, Hannah Baek, Chris Barrett, Golda Barrow, Richard Beckman, Parantapa Bhattacharya, Jiangzhuo Chen, Clark Cucinell, Patrick Corbett, Allan Dickerman, Stephen Eubank, Stefan Hoops, Ben Hurt, Ron Kenyon, Brian Klahn, Bryan Lewis, Dustin Machi, Chunhong Mao, Achla Marathe, Madhav Marathe, Henning Mortveit, Mark Orr, Joseph Outten, Akhil Peddireddy, Przemyslaw Porebski, Erin Raymond, Jose Bayoan Santiago Calderon, James Schlitt, Samarth Swarup, Alex Telionis, Srinivasan Venkatramanan, Anil Vullikanti, James Walke, Andrew Warren, Amanda Wilson, Dawen Xie

